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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,069	12/04/2003	Carsten Muenk	532792000100	9175

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EXAMINER

HUMPHREY, LOUISE WANG ZHIYING

ART UNIT PAPER NUMBER

1648

DATE MAILED: 03/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/729,069	<b>Applicant(s)</b> MUENK ET AL.	
	<b>Examiner</b> Louise Humphrey, Ph.D.	<b>Art Unit</b> 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 06 February 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 21 is/are pending in the application.
- 4a) Of the above claim(s) 3, 7 and 8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-6, 9-14 and 21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 December 2003 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### DETAILED ACTION

This Office Action is in response to the amendment and arguments filed on 06 February 2006 and the phone interview with Attorney Bruce Grant on 07 March 2006.

Claims 1, 2, 4-6, 9-14, and 21 are pending. Claim 21 is newly added. Claims 15-20 are canceled. Claims 3, 7, and 8 are withdrawn as being drawn to nonelected species. Claims 1, 2, 4-6, 9-14, and 21 are rejected. No claim is allowable.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 1, 2, 4-6, and 9-14 under 35 U.S.C. §103(a) as being obvious over Bieniasz *et al.* (1997) in view of both Wigley *et al.* (2001) and Isaacs *et al.* (1999) is **withdrawn** in view of Attorney Grant's contention during the phone interview regarding the lack of reasonable expectation of success in changing the intracistronic alpha and omega complementation of the reporter gene of Wigley *et al.* to the instantly claimed cell-fusion-dependent alpha and omega complementation or reporter gene.

Applicants' arguments filed in paper on 06 February 2006 have been fully considered but are not persuasive. However, during the phone interview on 07 March 2006, Attorney Grant further elaborated the alleged difference between the claimed cell fusion reporter gene system and the Wigley reporter gene system by noting that the alpha and omega fragments of the reporter gene in the claimed method are placed in two separate cells, as opposed to in the same cell as taught by the Wigley reference. Wigley teaches reporter gene complementation in the same bacterial cell whereas the

Art Unit: 1648

claimed method is practiced in two separate mammalian cells. A eukaryotic cell structure differs from a prokaryotic cell structure. Based on this fact, Attorney Grant speculated that mammalian cell fusion might release proteases, which may destroy reporter gene fragments, and therefore, simply separating the reporter fragments of Wigley into two separate cells of any kind would not establish reasonable expectation of success.

The following is a new ground of rejection:

***Claim Rejections - 35 USC § 103***

Claims 1, 2, 4, 5, and 9-14 are rejected under 35 U.S.C. §103(a) as being unpatentable over Bieniasz *et al.* (1997) in view of Mohler *et al.* (1996).

Claims 1, 2, 4, 5, and 9-14 are directed to a method for detecting the presence or absence of cell fusion, comprising contacting a first cell and a second cell, wherein the first cell comprises a first reporter molecule fragment and a viral envelope protein; the second cell comprises a second reporter molecule fragment and a viral envelope protein receptor. When the first and second fragment of reporter molecule is combined into one functional reporter gene, a chemiluminescent signal of cell fusion is emitted. Claim 2 further limits the reporter gene to  $\beta$ -galactosidase ( $\beta$ -Gal).

Bieniasz *et al.* discloses a 293T cell co-expressing CD4-CCR5-  $\beta$ -Gal and a second 293T cell expressing an HIV envelope protein (page 2600, left column, Results).

Bieniasz *et al.* does not disclose the complementation of the alpha and omega fragment of  $\beta$ -Gal.

Mohler *et al.* discloses the complementing of  $\beta$ -Gal alpha and omega fragments as biological indicators of cell fusion. See page 12425, Figure 2.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to modify the  $\beta$ -Gal of Bieniasz such that the reporter gene is split into two fragments expressed by two separate cells to be tested in a fusion assay rather than expressing the full length reporter gene in a single cell. One having ordinary skill in the art would have been motivated to do this so that the complementation of the reporter gene does not occur between adjacent single transduced cells, indicating that cell fusion is a prerequisite for the formation of complemented enzyme (page 12426), as per the suggestion in Mohler *et al.*, which specifically states that "the complementing properties of mutant lacZ genes can be exploited for a wide range of studies" and is broadly applicable. See page 12427, Conclusions. In other words, this modification of the cell fusion assay reduces false positive signals and increases the accuracy of the method. The working examples disclosed in Mohler *et al.* provide one skilled in the art with a reasonable expectation of success. Thus, claims 1, 2, 4, 5, and 9-14 are obvious over Bieniasz *et al.* in view of Mohler *et al.*

The following new ground of rejection is necessitated by the amendment.

The instant claims further limit the instant invention to comprise a molecule that inhibits cell fusion.

Moir *et al.* discloses a first cell co-expressing CD4- $\beta$ -Gal and a second cell expressing HIV-1 envelope protein and Rev (page 812, Materials and Methods). Moir *et al.* suggests applying this fusion assay system to the search for potential fusion blocking agents (last sentence).

Moir *et al.* does not disclose the complementation of the alpha and omega fragments of  $\beta$ -Gal.

Mohler *et al.* discloses the complementing of  $\beta$ -Gal alpha and omega fragments as biological indicators of cell fusion. See page 12425, Figure 2.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to modify  $\beta$ -Gal of Moir such that the reporter gene is split into two fragments expressed by two separate cells to be tested in a fusion assay rather than expressing the full length reporter gene in a single cell. One having ordinary skill in the art would have been motivated to do this so that the complementation of the reporter gene does not occur between adjacent single transduced cells, indicating that cell fusion is a prerequisite for the formation of complemented enzyme, as per the suggestion in Mohler *et al.* In other words, this modification of the cell fusion assay reduces false positive signals and increases the accuracy of the method. The working examples disclosed in Mohler *et al.* provide one skilled in the art with a reasonable expectation of success. Thus, claims 1, 2, 4, 5, and 9-14 are obvious over Moir *et al.* in view of Mohler *et al.*

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Louise Humphrey  
8 March 2006



**JEFFREY STUCKER**  
**PRIMARY EXAMINER**